



## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

### CERTIFICATE OF MAILING

I hereby certify that this REQUEST and the documents referred to as enclosed therein are being deposited with the United States Postal Service on the date indicated below with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450; Alexandria, VA 22313-1450.

Ariel Fletcher

Ariel Fletcher

12/21/2003

Date of Deposit

Applicant:	Brooks, et al.	)	
		)	
Serial No.:	09/081,522	)	Group Art Unit: 1644
		)	
Filed:	May 19, 1998	)	Examiner: P. Gambel
		)	
Title:	INHIBITION OF ANGIOGENESIS IN DISEASE STATES WITH AN ANTI- $\alpha$ v $\beta$ 3 MONOCLONAL ANTIBODY (AS AMENDED)	)	Confirmation No. 1607
		)	
		)	Our Ref.: TSRI 419.0 Con 1
		)	

### **FOURTH SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. §1.56 and §1.97**

In accordance with the continuing duty of disclosure imposed by 37 C.F.R. § 1.56 and § 1.97 to inform the Patent Office of all references coming to the attention of each individual associated with the filing or prosecution of the subject application, which are or may be material to the patentability of any claim of the application, Applicants hereby direct the Examiner's attention to the references listed on the attached revised form PTO-1449 entitled "List of References Cited by Applicant." A legible copy of the fifteen attached references are being submitted herewith.

Identification of the listed references is not to be construed an admission of Applicants or Attorneys for Applicants that such references are available as "prior art" against the subject application.

Applicants respectfully request that the Examiner review the foregoing references and that the references be made of record in the file history of the application.

Since this Supplemental Information Disclosure Statement is being filed before the mailing date of the first Office Action after the filing of a Request for Continued

Examination under §1.114, the fee required to be filed with the accompanying Supplemental Information Disclosure Statement has been estimated to be \$0.00. However, should the Patent Office determine otherwise, please charge the required fee to Deposit Account No. 19-0962. A copy of this sheet is enclosed for accounting purposes.

December 29, 2003

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Date

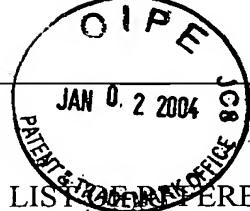
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Respectfully submitted,



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**LIST OF REFERENCES CITED BY APPLICANT**  
(Use several sheets if necessary)

ATTY DOCKET NO. **TSRI 419.0 C1** APPLICATION NO **09/081,522**

APPLICANT  
**Brooks et al.**

FILING DATE **05/19/98** GROUP **1644**

**U.S. PATENT DOCUMENTS**

*EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
A01	5,578,704	11/26/96	Kim			
A02	5,652,109	7/29/97	Kim			
A03	5,652,110	7/29/97	Kim			
A04	5,677,181	10/14/97	Parish			
A05	5,874,081	02/23/99	Parish			

**FOREIGN PATENT DOCUMENTS**

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION
B01	WO 94/10331	5/11/94				YES NO

**OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)**

C01	Adams et al., "Increased Affinity Leads to Improved Selective Tumor Delivery of Single-Chain Fv Antibodies," <u>Cancer Research</u> 58: 485-490 (1998).
C02	Carmeliet, "Integrin indecision," <u>Nature Medicine</u> 8: 14-16 (2002).
C03	Cheresh, "Human endothelial cells synthesize and express an Arg-Gly-Asp-directed adhesion receptor involved in attachment to fibrinogen and von Willebrand factor," <u>Proc. Natl. Acad. Sci USA</u> 84: 6471-6475 (1987).
C04	Cheresh et al., "Integrin-mediated death: An explanation of the integrin-knockout phenotype?" <u>Nature Medicine</u> 8:193-194 (2002).
C05	Posey et al., "Pilot Trial of Vitaxin, A Humanized Anti-Vitronectin Receptor (anti $\alpha_v\beta_3$ ) Antibody in Patients with Metastatic Cancer," <u>Cancer Biotherapy &amp; Radiopharmaceuticals</u> 16: 125-132 (2001).
C06	Rader et al., "Phage display approach for rapid antibody humanization: Designed combinatorial V gene libraries," <u>Proc. Natl. Acad. Sci. USA</u> 95: 8910-8915 (1998).
C07	Reynolds et al., "Enhanced pathological angiogenesis in mice lacking $\beta_3$ integrin or $\beta_3$ and $\beta_5$ integrins," <u>Nature Medicine</u> 8: 27-34 (2002).
C08	Schier et al., "Isolation of High-affinity Monomeric Human Anti-c-erbB-2 Single chain Fv Using affinity-driven Selection," <u>J. Mol. Biol.</u> 255: 28-43 (1996).
C09	Schier et al., "Isolation of Picomolar Affinity Anti-c-erbB-2 Single-chain Fv by Molecular Evolution of the Complementarity Determining Regions in the Center of the Antibody Binding Site," <u>J. Mol. Biol.</u> 263: 551-567 (1996).

EXAMINER

DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.